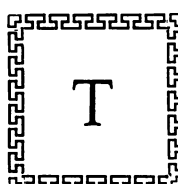


## THE GENESIS OF ATHEROSCLEROSIS\*

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**T**HERE is a great deal of confusion in the minds of both the medical profession and the nonmedical public with respect to the topic of atherosclerosis—its causes and the possibilities of prevention. I hope not to increase this confusion. Further, even if I do not succeed in clarifying the problem for you, we can, at least, make some attempt to outline the basic issues. In recent months, the lay press has carried a series of confusing stories emanating from statements released by the American Medical Association. The major confusion has arisen as a result of the statement on dietary fats which appeared in the *Journal of the American Medical Association* in August of 1962.<sup>1</sup> This was intended for professional use only. It was a very clear, concise, and excellent presentation of the story.

The attempt on the part of many people at “do-it-yourself” dieting brought forth a storm of protest from a group within the Association. This resulted in a second news release in October of 1962. At first reading, this second release was contrary and contradictory to the basic scientific story as presented by the Council on Foods and Nutrition of the American Medical Association. The chairman of the Council prepared an editorial clarifying this issue. This editorial appeared in a recent issue of the *J.A.M.A.* and unequivocally stated the position of the Council, as expressed in the scientific article of August, 1962, “. . . that there is a very definite relationship between the serum cholesterol concentration and dietary patterns and habits. . . .” The unknown part of the story is whether or not, by proper control of the serum cholesterol concentration, the incidence of coronary heart disease can be decreased. The Council went on further to point out that certainly no harm can come from the dietary controls which will result in a de-

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This article is a review for instructional purposes and credit to the many investigators involved in the subject has not been included.

TABLE I.—CLASSIFICATION OF LIPIDEMIAS\*

A. Hypertriglyceridemia with Hypercholesterolemia
1. Carbohydrate-Induced
2. Fat-Induced
3. Caloric Excess
4. Neither Fat- nor Carbohydrate-Induced
5. Alcohol-Induced
B. Hypercholesterolemia with Hypertriglyceridemia usually associated with abnormal <i>glucose-tolerance</i> test or family history of abnormal glucose metabolism
C. Hypercholesterolemia with Normal Triglyceride Concentration (High Beta-Lipoprotein)
1. Genetic

\* The author's synthesis of discussions held at the Duell Conference on Lipids, February, 1963. The author also assumes responsibility for this version of these discussions.

creased serum cholesterol concentration, and, therefore, they advised control of serum cholesterol as good, prudent practice at the present time. Basically, the dietary changes recommended are the substitution for the saturated fats in the diet by the polyunsaturated vegetable oils. For the remaining time I shall attempt to discuss the simplicities with which one can approach this basic problem.

One way of solving a complex problem is to break it down into its component parts. Each part is approached as a specific problem, and, as the solution to each is found they are gradually integrated back into the problem as a whole. At first, many gaps will trouble us—but gradually these will be filled in and the answer to the whole problem will eventually be found.

In this particular problem of atherosclerotic vascular disease, the ultimate therapeutic approach will depend upon an understanding of the etiological or causative factors. The first step in the study of the cause is to find possible associated factors. The elegant techniques of the epidemiologist have been applied toward this end. I shall not dwell on this aspect of the problem tonight as Dr. Stamler, in a subsequent lecture in this series, will develop this part of the problem in a complete presentation. Sufficient to say that a positive statistical association has been found between blood lipid concentration and the incidence of coronary artery heart disease.

TABLE II.—PRIMARY CHYLOMICRONEMIA

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|----|---|
| A. | Familial — Early in life — Occurs equally in both sexes |
| B. | Due to Lipoprotein Lipase Deficiency                    |
| C. | Normal Cholesterol Concentration                        |
| D. | Not Associated with Vascular Disease                    |
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The next step, then, is to study the factors which influence the blood fat concentration. Tonight I shall try to concentrate on this aspect of the problem. I have for your information a suggested classification of the lipidemias (Table I). There will probably be as many classifications as there are people attempting to write them. In the first category we have put hypertriglyceridemia with hypercholesterolemia (Table I-A). This is the most common. It is associated, most likely, with high carbohydrate intake, surprising as it may seem. It can be induced by high fat intake under many conditions. It is frequently associated with caloric excess. However, there are types of this hypercholesterolemia which are associated with neither fat nor carbohydrates. Also, of course, we have the type which is associated with an excessive consumption of alcohol.

The second class is the hypercholesterolemia with hypertriglyceridemia (Table I-B). You will recall the first was hypertriglyceridemia with hypercholesterolemia. This second class accents the hypercholesterolemia. This is usually associated with an abnormal glucose-tolerance test or a family history of abnormal glucose-tolerance test. In other words, it is the type of hyperlipidemia which we see in diabetic patients and in people who have a strong family history of diabetes.

The third type is the hypercholesterolemia with normal triglycerides (Table I-C). This group includes those who have a high beta lipoprotein concentration—and this is undoubtedly purely genetic in origin. The gene is a penetrating one, and when it occurs on both sides of the family, then the incidence is practically 100 per cent in the sibling.

Table II shows further categories of this, the primary chylomicronemias. The chylomicrons are the visible fat droplets in the blood. Any particulate matter which is large enough to diffract light producing the milky opalescence is associated with these chylomicronemias. This primary chylomicronemia is a familial characteristic. It is seen early

TABLE III.—EXOTIC FORMS OF HYPERTRIGLYCERIDEMIA

- |  |
|--|
| A. Tangiers Disease. Low Alpha-Lipoprotein |
| B. Niemann-Pick                            |
| C. Acanthoses                              |
| D. Hepatic Hypercholesterolemia            |

in life, frequently in infants, and it occurs equally in both sexes. It is probably due to a lipoprotein lipase deficiency, and the cholesterol concentration is normal. This type of hyperlipidemia is not associated with vascular disease.

Table III presents what we call the exotic forms of hypertriglyceridemia. The first is due to a low alpha-lipoprotein. It was first found by Frederickson of the National Institutes of Health in a family group on one of the islands off the coast of Maryland in Chesapeake Bay, the island of Tangiers, which has given its name to the disease.

Also included in this group are the classic Niemann-Pick disease, the acanthoses and the hepatic hypercholesterolemias.

This grouping represents an attempt to categorize and to prepare a taxonomy of the clinical syndromes associated with the hyperlipemias or, particularly, the hypertriglyceridemias with cholesterol. The form in which the triglycerides are carried in the blood is most important. This importance lies in its relationship to its being a possible etiological factor in vascular disease. The triglyceride must be associated with a high cholesterol. The size of the particle which is carrying both the cholesterol and the triglyceride is important. The configuration of the particle—and particularly the strength of the bonding holding the lipid and protein together—are most important as total determinants in this field.

Based upon this attempt to categorize the hyperlipidemias, we can derive a concept of therapy. This therapeutic approach should be based upon causal factors. Most of the hypertriglyceridemias with hypercholesterolemia are carbohydrate-induced. This is indeed important to recognize in the development of the therapeutic diets. The diet of choice, then, is limited in carbohydrates and, because of the associated high cholesterol concentration, usually should contain a high polyunsaturated fatty acid concentration (Table IV).

TABLE IV.—THERAPY

Approach Must Be Based on Causal Factors	
Most Hypertriglyceridemias with Hypercholesterolemia are Carbohydrate-Induced.	
Diet of Choice:	Limited Carbohydrate High Polyunsaturated Fatty Acid

TABLE V.

A. CHOLESTEROL WIDESPREAD IN MAMMALIAN VERTEBRATES	
Muscle	Spinal Cord
Liver	Egg Yolk
Blood Plasma	Butter
Brain	Lard
B. CHOLESTEROL ABSENT IN:	
1. Plant Tissues	
2. Shell Fish (Crabs, Shrimps, Oysters)	

What is cholesterol? Perhaps no other chemical substance has been so widely discussed, nor has any chemical substance been so widely misunderstood as this complex cyclic alcohol. The name cholesterol is derived from the Greek, from *chole*, meaning bile and *steros*, meaning solid. It was a substance first identified as a constituent of gall stones. Cholesterol is a solid, is white in color, waxy in appearance, and is classed as a lipid because it is soluble in fat and in those solvents which dissolve fats. It is widely spread throughout all mammalian tissues. It is found in muscle, liver, blood plasma, brain, spinal cord, egg yolk, butter, lard, and so forth (Table V-A). Cholesterol does not occur in plant tissues, nor in shellfish, such as crabs, shrimps, or oysters (Table V-B). Plants and shellfish, however, do contain sterols which are very similar in chemical constitution, but are sufficiently different to have entirely different impacts on metabolism. The plant sterols are, in fact, not only poorly absorbed by humans, but actually interfere with the absorption of cholesterol from the human gastro-intestinal tract. This fact has been utilized in one of the chemotherapeutic attempts to control human serum-cholesterol concentration, that is, by feeding of

TABLE VI.—CHOLESTEROL IS IMPORTANT

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1. In Biosynthesis of Sex Hormones
  2. In Biosynthesis of Adrenal Cortical Hormones
  3. In the Transport of Essential Fatty Acids
  4. In the Skin and in Forming the Covering of Nerve Fibers
- 
- 

the plant beta-sitosterol. Aside from these broad statements about cholesterol, there are two very particular facts which are of special interest to us. First, cholesterol is found to be a major constituent of the atherosclerotic plaques; and secondly, it was a Russian scientist, Anitschkow, who, about fifty years ago, fed cholesterol to rabbits and produced atherosclerosis in these animals in the laboratory.

Cholesterol in the human body is derived from two sources: (a) from the food we eat, and (b) it is manufactured or synthesized by the tissues in our body.

The average American diet contains between 500 and 800 mgm. of cholesterol each day. The presence of other fats in the diet increases the absorption of this cholesterol. The biosynthesis of cholesterol occurs in almost every tissue of the body, but the major site of this production is in the liver. Cholesterol is manufactured from the acetate radical, the two-carbon fragment, which results from the breakdown of both carbohydrates and proteins, as well as from the breakdown of the long-chain fatty acids. The biosynthesis is a very complex process and goes through a great many stages which have been clearly defined and specifically identified in the laboratory. Of the many factors which influence the rate and degree of cholesterol biosynthesis, the diet is the most important. Starvation, or fasting with a limited caloric intake, decreases cholesterol synthesis, particularly by the liver. The ingestion of large amounts of cholesterol in the diet also decreases this biosynthesis. Many attempts to control the biosynthesis of cholesterol by blocking the procedure at various stages have been tried and some have been successful. One of the recent chemotherapeutic agents, Mer-29, did exactly this. However, it blocked it at a point where a new sterol was formed, which resulted in general toxic manifestations. One must not, however, look upon cholesterol only as a villain. It is extremely important in the manufacture of the sex hormones and of the adrenal cortical hormones.

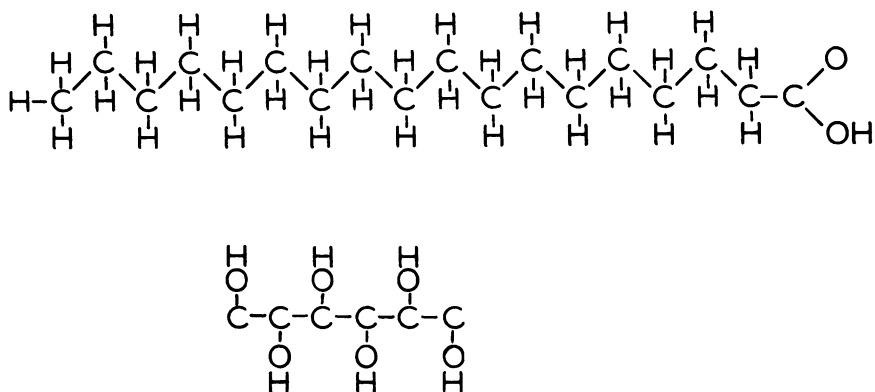


Fig. 1

A (above) Stearic Acid  
 B (below) Carbohydrate

It is also very important in the transport of the essential fatty acids. The fact that it is present in the covering of nerve fibers and in the skin is indicative that it must have most important life-saving functions (Table VI).

The concentration of cholesterol in the blood, then, is the resultant of the over-all cholesterol metabolism; that is, that which comes from the diet, and that which is manufactured in the body, less that amount which is utilized or excreted.

It has been mentioned that the modification of the fat content of the diet has an impact on the concentration of cholesterol in the circulating blood. The major changes that are recommended are control of the caloric intake, the maintenance of optimum weight, and control of the type and amount of fat in the diet. Basically, there are two kinds of fatty acids for the purposes of this discussion. These are the saturated and the unsaturated fatty acids. The latter group is divided further into the monounsaturates and the polyunsaturates.

From a knowledge of the physical and the chemical properties of these compounds, it is quite frequently possible to explain, and even to predict, the physiological properties that they will have in the human metabolic cycles. The dietary fatty acids are classical examples of this ability to predict the activities of a nutrient.

If we consider the structure of the fatty acids, it will be seen that



Fig. 2. Interlocking fit of molecules. A dense compound, high melting point, solid at room temperature.



Fig. 3. Oleic Acid. Lower melting point, semi-solid at room temperature, greater degree of solubility.

the saturated fatty acid shows a molecular structure that is linear or extended.

If we consider specifically stearic acid, the 18-carbon chain compound, it is apparent that 17 of these are joined by single bonds, one to the other; and the end group, the oxidated carbon or the carboxyl group, is there for purposes of reactivity with other compounds (Figure 1-A). The 17 carbons with their component 35 hydrogens are in a very low state of oxidation—there are no oxygen molecules present. Therefore, the maximum amount of energy is obtained by combustion. In contrast, the carbohydrates, in which every molecule contains an oxygen atom, the energy available, while more readily and more freely accessible, is less than half of that contained in an equivalent weight of fatty acids (Figure 1-B). Hence, we say that fatty acids have high-energy densities. Thus, the fats are a prime source of energy in our diet. The extended or straight-line shape of the molecule allows the other molecules to fit into each other in an interlocking pattern. This means that this is a dense compound and it will have a relatively high melting point which makes it solid at room temperature, a characteristic of fats (Figure 2). It will be relatively insoluble because of the inability of the solvents to break the bond forces between these molecules. Now, if we introduce a double bond into the formation of this, we have a single double bond which results in a bend in the molecule (Figure 3). This is oleic acid.



TABLE VII.—FOODS HIGH IN POLYUNSATURATED FATTY ACIDS

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Vegetable Oils (Cotton seed, Corn, Safflower, Soybean)
Fish
Fowl

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tween these two basic sources. The seed fats, by which I mean the oils derived from cotton seed, soybeans, and the kernels of corn, are rich in the polyunsaturated acids. There are, however, vegetable-origin fats which do not follow this pattern. These are, particularly, the avocado and the olive, which are of the same family; and they are high in the monounsaturates, but extremely low in the polyunsaturates. Coconut oil is extremely low in both mono- and polyunsaturates. So, it is apparent that it is quite possible to have vegetable-origin oils and fats which are not polyunsaturated; and, therefore, it is not fair to speak of the vegetable oils or the animal fats as being exclusively saturated or polyunsaturated.

Animal fats, on the other hand, particularly those which are derived from the ruminant animals, such as the cow and the sheep, have a very high percentage of saturated fatty acids. In the vegetable oils, the polyunsaturated fatty acids are high in the cotton seed, corn, safflower and soy bean oils—but the polyunsaturated fatty acids are also quite high in fowl and fish (Table VII). Fowl and fish are in contrast to the ruminants, which are high in saturated fatty acids. The ruminants are the common edible animals we have in our economy. The human and the pig have a variable composition in their fats, depending upon their diet. The ruminant converts all fat into the saturated fat, because he has a very efficient hydrogenating mechanism, his “fermentation chamber”. The human, the chicken, the pig, on the other hand, the direct pepsin-digestive group, do not hydrogenate their fats and as a result their depot fat reflects, to a very large extent, the fats which are consumed in the diet. There was a time, for example, during World War II when the hog economy in this country called for the feeding of peanuts to hogs instead of the standard hog feeding. The peanut is high in polyunsaturates and, as was pointed out, the polyunsaturates are liquid at room temperature. This gave rise to the so-called “soft” hams and “runny” lards.

The American public is not accustomed to having soft lard or greasy-looking hams. Consequently, this type of ham and bacon did not receive wide acceptance and feeding the hogs with peanuts was purely a war-time measure. Just as soon as the usual animal feeds became available, the farmers reverted to this type of hog feeding, to supply the more solid hams and lards to which the American public was more accustomed. But it does point out that the hog fat and the lards as they were formerly used, in the 16th, 17th, 18th and even the early part of the 19th centuries, were fairly high in the polyunsaturated fatty acids. The old literature is full of all sorts of techniques and schemes used to make lard firm so that it could be shipped in commerce. This was an indication of its high polyunsaturated qualities, as previously noted.

The simple substitution of fish and fowl, and even of pork from hogs which have been fed on peanuts, is a long stride towards introducing the polyunsaturated fatty acids into the diet in preference to the saturated fats, when this is indicated. With regard to beef, the lean meats are to be preferred to the fat beefs because of the lower saturated fat content or the lower total fat content of lean beef.

To return to the question of the dietary modifications which are required in the attempt to control serum cholesterol concentration, it has been pointed out that this can be, in effect, a comparatively simple process. Lists of foods that are high in fat, low in fat, high in saturated fatty acids, and high in polyunsaturated fatty acids are available in all standard text books and from the Federal Department of Agriculture.

One of the most important sources of fat in the human dietary is the fat which is added in the cooking process, as in deep-frying or pan frying, larding, salad oils, and so on.

The restriction of dietary fat, or the introduction of the so-called low-fat diet, must be done with a great deal of caution. First of all, fatty foods carry with them the fat-soluble vitamins A, D, E, and K. These are essential for human nutrition and any dietary modification which eliminates these vitamins from the diet, or minimizes the ability of the body to absorb them from the gastro-intestinal tract, would interfere with good nutrition. In addition, carotene, which is the pro-vitamin A, is contained in our dietary fat to a large extent and certainly is absorbed from the intestinal tract, preferably in the presence of dietary fat.

In calculating a diet or in prescribing a diet, one must first make provision for the calories that are necessary for the individual. No diet which is inadequate in calories is satisfactory. One may have a boxcar full of vitamins, one may have loads of polyunsaturated fatty acids—but if the caloric requirements are not satisfied, then starvation will ensue. If one attempts to reduce the total fat of the diet beyond this optimum point of adequate calories, then the calories must be derived from other sources. The only two possible other sources are the proteins and carbohydrates. We know that there is a limit to the amount of protein which people will eat or can eat, because of the high satiety value which protein foods carry with them, and because it is economically not feasible to consume more than the optimum of protein during the course of the day.

Aside from the fats, the carbohydrates are the cheapest source of calories. If one increases the carbohydrate content of the diet to a high level, this carbohydrate is metabolized in the body through the fat mechanisms. We pointed out earlier that one of the basic causes of hyperlipidemias is a high carbohydrate intake. This is, as stated, not only because the carbohydrate is metabolized in the body through the fat mechanism, but also because the only type of fat that the body can manufacture from carbohydrates is a *saturated* fat. So, in effect, a high carbohydrate diet becomes, metabolically speaking, a high saturated fat diet. This may be why a high carbohydrate intake is associated most frequently with these hyperlipidemias, both of the triglyceride type and of the cholesterol type. This has been shown very definitely to be so by many well-controlled experimental approaches. Therefore, one must make provision for definite amounts of fat in the diet in order to keep the proportions of fat at an optimum level. One must include fat in the diet not only to keep these optimum levels but also to prevent this surplus amount of carbohydrate from being converted to a saturated fat in the body.

Since one must include fat in the diet, an attempt should be made to keep the polyunsaturated fatty acid content consistent with the end that one wants to achieve. The diet must be practicable and palatable, otherwise the individual will not consume it and the whole regime will fail to accomplish its purpose. These modifications can be comparatively simple when trying to increase the polyunsaturated fatty acids in the diet. As stated previously, the vegetable oils—cotton seed, corn,

safflower—are the common items of food which are high in the linoleic acid or polyunsaturated fatty acid. The use of these oils in salad, in food preparation, as in frying, is simple and effective, and increases the polyunsaturated fatty acid content of the diet. In recent years there has been an attempt to prepare special foods which are high in polyunsaturated fatty acids. One of the major eating habits of the people of this country is to spread something on bread. Butter, as we know, is one of those fats which increases the cholesterol content of the blood. Therefore, innumerable special margarines have been prepared which purport to have high polyunsaturated fatty acid content. Many of those which claim this property do not have it. There are, however, several excellent preparations available which do contain adequate quantities of the polyunsaturated fatty acids. By reading the labels carefully the housewife can discriminate between those which fulfill the promise and those which do not. Basically, if the oil is hydrogenated directly it will not have as high a polyunsaturated fatty acid content as if the liquid oil is mixed with what is called a matrix, because the problem, as you will remember, is that the polyunsaturated fatty acids are liquid at room temperature, and the manufacturers are attempting to incorporate this into some type of preparation which will keep it solid so that it can be spread on bread.

Let us review briefly some of what has been said up to this point. A great deal of evidence has been accumulated from a variety of reliable sources to indicate that there is a relationship between the diet, as consumed by people, and the concentration of total fat, and particularly cholesterol in the blood, and atherosclerotic coronary heart disease. Based upon this association, many physicians have accepted the hypothesis that the modification of the fat of the diet can be used to reduce the concentration of fat and cholesterol in the blood, and that this would have an impact on both the incidence and the severity of atherosclerosis. The first part of the hypothesis, that is, the effect of diet on blood lipids, has now been proved beyond any question of doubt, and most people accept it. The second part of the hypothesis, i.e., that by modifying the diet one can prevent or reduce atherosclerosis, has not been demonstrated to date to the complete satisfaction of all concerned. The Framingham study results, as published by the United States Public Health Service, indicate the positive correlation between the concentration of cholesterol in the blood, blood pressure, obesity, and coro-

nary artery heart disease. There have been fragmentary reports from several sources to indicate that the second part of the hypothesis outlined above, does have a good deal of evidence to support it.

Since many people object to dietary modification, attempts are being made to simplify the life of those who will have to adhere to altered dietary regimes and to make it easy for them to continue in their basic dietary pattern, and at the same time obtain the benefit of this modification. In a recent issue of the *J.A.M.A.*, the research group of the Cleveland Clinic had an article on the use of fat-modified foods for serum cholesterol reduction.<sup>2</sup> The Cleveland group obtained the cooperation of food processors and manufacturers who prepared specific foods to their specifications. Their over-all objective was to restrict markedly the intake of saturated fatty acids, while increasing the amount of dietary polyunsaturated fatty acids. They knew well that the American public did not like to reduce the total amount of fat in the diet and their dietary design was such as to maintain the total fat intake at the usual level. By a meticulous technique of dispensing these foods at reduced prices through a commissary, they were able to get many married first- and second-year students at the medical school to participate in this study. Altogether, 55 volunteered and were suitable for the study they undertook. The instructions given to these couples were quite simple. They were given a list of foods that they were not to eat. They were also given a list of foods that they could eat, and they were instructed to use only polyunsaturated vegetable oils in food preparation and in salads. They were then given the privilege of purchasing at the commissary, at reduced prices, these modified or fat-filled foods. The special foods, particularly the meats, were carefully prepared; and those parts containing the saturated fatty acids were removed at the processing plants. This was done by closely trimming meats, and by skimming procedures during the cooking process. Other foods were filled with polyunsaturated acids, that is, by replacing the saturated fat with liquid vegetable oils. These foods included milk, the cheeses, the sour creams, ice cream, and such meat products as hamburger, bologna, sausage and frankfurters that were amenable to this type of processing. Bakery products were prepared with the polyunsaturated vegetable oils, as were the special casseroles and other extended mixed foods. Their conclusion was that their efforts to substitute polyunsaturated fatty acids for saturated fats were, in general, successful. The mean

decrease in the serum cholesterol concentration under these carefully controlled conditions was 14 per cent and this was maintained throughout the course of the study without any evidence of a rebound effect. This compares favorably with the work done in other groups.

To review, then, the Cleveland experimental group stated that a large variety of common fat-containing foods can be modified by food processing and the saturated fats can be deleted and, in many instances, they can be replaced with the polyunsaturated oils. They had a significant reduction in the serum cholesterol concentration by this dietary manipulation over a 10-month period.

In New York City, over a period of six years, an experiment has been conducted called "The Anti-Coronary Club". This was first conceived by the late Dr. Norman Jolliffe and has been carried out successfully over an extended period of time. On this occasion time does not permit a detailed discussion of the entire experiment. Suffice it to say that this work has been carried on further and the current conclusions are that this "prudent diet", as Dr. Jolliffe called it, basically, the substitution of the polyunsaturated fatty acids in the form of fowl, fish, lean beef, for the fatty saturated acids and the use of "filled" milks and ice creams, and the use of polyunsaturated oils for cooking and salad dressings, will significantly lower the serum cholesterol concentration. While a study of the evidence and of the rate of incidence of coronary heart disease occurring among those who had adhered to this diet does not prove that a decrease in serum cholesterol will lower the incidence of coronary heart disease, the investigators have, nevertheless, been encouraged to continue this study. A comparison of their results with the expected incidence of coronary heart disease, as based on the Framingham Study, leads them to believe that their efforts have had some favorable impact on the solution of this problem in the patients of this experimental group.

This is being followed through and in the course of time we shall hear from it. As many of you know, and as has been reported in the newspapers recently, there is now a feasibility study being started, supported by the U.S. Public Health Service, in five major clinical centers throughout the country, to determine whether or not large-scale applications of this type of dietary modification: 1) are feasible; and 2) whether or not they are effective. Results from these tests will take many years, of course, to bring returns.

In summary, then, there is a proven statistical association between hyperlipidemia and atherosclerotic vascular disease. Hyperlipidemias may be due, basically, to increased cholesterol, cholesterol with triglycerides, and triglycerides with cholesterol. Primary hypercholesterolemia with normal triglycerides is related to very definite inherited genetic factors. The garden-variety of hyperlipidemia is basically due to excessive calories and to high carbohydrate intakes. Most hyperlipidemias can be influenced by dietary manipulation, consisting basically of an average fat content of about 40 per cent of calories, and by substitution of polyunsaturated oils for the saturated fats. The impact of the control of serum lipids on the prevention of atherosclerotic heart disease has not, as yet, been proven; but, there is indicative evidence that makes it imperative that this subject be pursued with vigor.

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